Title: Prothrombin complex concentrate versus fresh frozen plasma in adults undergoing heart surgery (PROPHESY) - a pragmatic pilot randomized controlled trial

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Background: Fresh Frozen Plasma (FFP) is the standard treatment for clotting factor replacement in bleeding patients undergoing cardiac surgery in the UK. However, prothrombin complex concentrate (PCC) is being used off-license in this setting due to higher concentration of clotting factor levels, smaller volume, and more rapid administration as compared to FFP. **Method**: PROPHESY is a pragmatic single-centre, pilot randomized, controlled trial (RCT) that assessed the feasibility of a large trial to compare FFP with PCC in cardiac surgery. The trial was registered on the EudraCT database (2018-003041-41) and Clinicaltrials.gov (NCT03715348). Primary outcome was to evaluate the proportion of subjects who are consented and receive the intervention. *Secondary objectives were to* assess the delivery of different components of the trial, protocol violation/compliance and ability to collect outcome data up to 90 days after surgery. *Inclusion criteria*: Adult patients (≥18years, not on vitamin-K antagonists) undergoing cardiac surgery who develop active bleeding that requires FFP transfusion within 24 hours of surgery, were randomized by the transfusion laboratory to FFP (15ml/kg) or PCC (500 IU if <60kg, 1000 IU if 61–90kg, 1500IU if >90kg) using block randomization. If bleeding continued after administration of the first study dose, standard care was administered (no subsequent PCC dose was given). Follow-up was 90 days after surgery. **Results**: From January 2019 to November 2019, 180 patients were screened, of which 134 were consented, 54 (40% recruitment rate) received an intervention (25 FFP and 29 PCC) and 50 were appropriately randomised (25 on each arm). Of those that were randomised, the median age was 66 years (SD 12), 64% were male and 76% (PCC arm) and 80% (FFP) had elective surgery. There were 18 trial protocol deviations relating to randomisation (n=10), intervention (n=3), documentation (n=2) and research blood samples collection (n = 3). In randomised patients 113 adverse events (55 PCC vs. 58 FFP) and 19 serious adverse events (6 in 5 patients for PCC vs. 13 in 8 patients for FFP) were reported. There was no increase in thromboembolic event relating to PCC. Mean days alive and out of hospital within 90 days was 71.8 (SE=1.8) for PCC and 73.8 (SE=1.7) for FFP. No randomised patients were withdrawn from the study, 5 were lost to follow-up and 4 died (2 FFP and 2 PCC). Follow-up data up to 90 days were collected in 89% of randomised patients. **Conclusion**: There have been no RCTs to date that have compared the efficacy/safety of FFP versus PCC in cardiac surgery patients who are bleeding and this pilot study demonstrates that it is feasible to perform a large trial in the future.